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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/888,268	06/22/2001	Pananchukunath Manoj Kumar	RLL-178US	8724

26815 7590 03/17/2005

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EXAMINER	
YOUNG, MICAH PAUL	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 03/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/888,268	KUMAR ET AL.	
	Examiner	Art Unit	
	Micah-Paul Young	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgment of Papers Received: Amendment/Response dated 06/01/04.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 1-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined disclosures of Munayyer et al (WO 99/62516 hereafter referred to as '516), Ayer et al (USPN 3,980,778 hereafter referred to as '778) and Liversidge et al (USPN 5,145,684 hereafter referred to as '684). Claims 1-9 are drawn to an oral formulation comprising loratadine particles with an average particle size between 0.1 and 15 microns. Claims 10-18 are drawn to a process of making the formulation of claims 1-9 where the drug is milled into a specific particle size.

4. '778 discloses various drug preparations including oral formulation comprising fillers, binders and lubricants. One of the active ingredients can be an antihistamine, where the agents are ball milled to a size below 5 microns (examples). The formulation establishes continuity

between the various dosage forms, and it would be within the level of skill in the art to apply the processing steps of one preparation to those of all preparations. The formulation includes lactose, methylcellulose, starch, and magnesium stearate (col. 11, lin. 44-53). '778 however does not name the specific antihistamine.

5. '516 discloses an oral syrup formulation comprising micronized loratadine in association with fillers, lubricants, and binders (examples). The reference discloses that the loratadine is micronized, yet does not disclose a particular particle size. It would be within the level of skill in the art to ball mill the antihistamine as seen in '778. A skilled artisan would be motivated to do so in order to increase the surface area and in turn affect the bioavailability.

6. As is well established in the art the rate of dissolution of a particle drug can increase with increasing the surface area, i.e. decreasing the particle size (col. 1, lin. 28-30 '684). '684 follows this line of thinking by decreasing the particles size of active agent by various methods including milling (col. 5, lin. 41- col. 6, lin. 56) in order to increase their surface are and in turn their bioavailability. The particles are reduced to 400 nm or 0.4 microns (abstract), and can include antihistamines (col. 3, lin. 68). A skilled artisan would have followed this motivation to mill the micronized particles of '516 as suggested by '778.

7. With regard to the claims recited specific surface areas, it is the position of the examiner that such limitation would be well within the level of skill in the art to determine through routine experimentation. Barring a showing of unexpected results of said particle size/surface are combination, the limitation is deemed non-critical and does not distinguish the claims over the prior art.

8. Therefore one of ordinary skill in the art would have been motivated to reduce the loratadine particles of '516 as shown in '778 and '684 in order to increase the surface area and bioavailability. It would have been obvious to a skilled artisan to combine the teachings and suggestions as such with an expected result of a stable, oral loratadine formulation with increased bioavailability.

Response to Arguments

1. Applicant's arguments filed 6/01/04 have been fully considered but they are not persuasive. Applicant argues that:

a. Ayer does not teach milling a steroid in order to increase its bioavailability.

b. Ayer only discloses particles sizes for ointment and not for tablets or capsules.

c. Munayyer does not teach increasing bioavailability

d. Liversidge does not teach increasing bioavailability

e. There is no motivation to combine the references.

2. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

3. Regarding argument a., applicant argues that Ayer does not teach an increased bioavailability, yet this limitation is not reflected in the claims. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the increased and improved bioavailability) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification,

limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The Examiner aggress with applicant, that is well known in the art that ointments and creams are milled to lower particle sizes in order to avoid a gritty feeling; however the Examiner submits that lowered particle sizes also contribute to increased surface area and improved bioavailability. This knowledge is also well known in the art. The increasing of surface area is a further motivation for decreasing particle size.

4. Regarding argument b., the Examiner agrees that Ayer is silent to the specific particle sizes of the oral formulations. However, the reference is suggestive of milling active agents into fine small powders. The reference is relied upon for its teachings of milling and suggestions of dosage forms.

5. Regarding c., it is the position of the Examiner that though the bioavailability of the formulation is not expressly taught by the reference, the fact that the formulation provides a more stable dosage form with decreased degradation would lend itself to an improvement in bioavailability since the formulation is allowed to remain in its intended form and allowed to exhibit its pharmokinetic properties to the patient. The Munayyer reference discloses an oral suspension comprising a micronized loratadine. This reference is relied upon for its disclosure of oral suspensions of micronized loratadine.

6. Regarding argument d. and e., it is the position of the Examiner that applicant has misinterpreted the presentation of the art. Ayer provides the teaching of a milled antihistamine of a particular particle size; Munayyer provides the specific antihistamine and a suggestion of small particle size carried from the Ayer reference. Liversidge teaches the milling drug particles coated with excipients can improve stability and improve bioavailability. The reference provides

the motivation to an artisan of ordinary skill to mill the loratadine of Munayyer as seen in Liversidge and apply the excipients of Ayer to provide an oral dosage form. It is for these reasons that the claims will remain obviated by the art.

Conclusion

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Micah-Paul Young whose telephone number is 571-272-0608. The examiner can normally be reached on M-F 7:00-4:30 every other Monday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on 571-272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Micah-Paul Young
Examiner
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MP Young

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